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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/649,944	08/28/2003	Ralph M. Ellison	CP380D	7142

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EXAMINER	
PAK, JOHN D	

ART UNIT	PAPER NUMBER
1616	

DATE MAILED: 06/26/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/649,944	ELLISON ET AL.	
	Examiner	Art Unit	
	JOHN PAK	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 April 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-11,13-17,19 and 20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-11,13-17,19 and 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

This Office action is in response to applicant's amendments and remarks of 4/12/2006.

Claims 1, 3-11, 13-17 and 19-20 are pending in this application.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1 and 3-8 stand rejected under 35 U.S.C. 102(e) as being anticipated by Zhang (US 6,720,011) for the reasons of record – see pages 3-4 of the Office action of 12/15/2005.

Applicant argues that Zhang "fails to provide any guidance whatsoever as to the efficacy of the compositions for lymphoma treatment." Applicant argues that Zhang's single working example is for leukemia treatment and Zhang's description of inhibition of DNA/RNA synthesis is limited to leukemia cells. Accordingly, applicant argues, Zhang "fails to actually teach that arsenic trioxide is efficacious for the treatment of lymphoma."

The Examiner cannot agree. Applicant's position can be framed as "the reference is not enabled" type of argument. However, such an argument is not persuasive under the present fact situation. For Zhang to be non-enabled for treatment

of lymphoma with arsenic trioxide, said treatment could not have been obtainable without undue experimentation. However, such a proposition is rather implausible given what Zhang already disclosed in the context of the state of the art at the time Zhang provided his disclosure.

Breadth of Zhang's disclosure: Arsenic trioxide for leukemia, hepatoma and lymphoma. Such a scope is substantially narrower than applicant's ambitious assertion of effective treatment of virtually every type of cancer known to mankind (see instant specification).

Nature of the invention: See above. Leukemia, hepatoma and lymphomas all have many known and FDA-approved drugs for treatments. Zhang is not claiming some incredible utility.

State of the prior art: See above. Lymphoma treatments are known, and arsenic has been disclosed in the prior art as having beneficial anti-cancer and anti-lymphatic cancer activity. See the cited art of record.

Level of one of ordinary skill: The level of skill is of the highest order since treatment of cancer patients requires at least an MD with a specialty in oncology.

Level of predictability in the art: While cancer treatment is not always predictable, Zhang's disclosure overcomes that by disclosing lymphoma treatment and providing clinical data for leukemia treatment. Further, see CN 1121807, which

discloses arsenic trioxide for lymphatic cancers. See also Li et al.[1], who provide clinical data for treatment of lymphomas with an arsenic trioxide-containing "Ailin-1." Within this prior art context, level of predictability in the art for Zhang's teaching of lymphoma treatment with arsenic trioxide would have been quite high.

Amount of direction provided by Zhang: Zhang explicitly discloses treating lymphoma with arsenic trioxide (column 1, lines 34-45 and 41-43). IV composition containing 1-10 g arsenic trioxide, sodium chloride and water is disclosed (column 1, lines 41-54). Effective daily dose of 10 ml of a composition containing 10 g/l of arsenic trioxide added to 500 ml of a 10% glucose solution is disclosed (column 2, lines 9-12), as well as a 0.1 wt% to 1 wt% arsenic trioxide containing compositions (column 2, lines 44-45). All such disclosures are in no way limited to leukemia treatment, as applicant may suggest. Those disclosures are broadly made with respect to all of Zhang's disclosed treatments. Further, Zhang provides clinical data with 110 leukemia subjects, which data spans 20 years of follow-up results (columns 2-3, in particular column 3, lines 21-26). In contrast, it must be noted that applicant fails to provide any clinical data whatsoever in the instant application. Even though applicant claims treatment of "lymphoma in a human" (emphasis added), applicant fails to provide any clinical data.

[1] Applicant's criticism of Li et al. in that "Ailin-1" is not identified in the article will be addressed hereinbelow in the second ground of rejection under section 103. The rebuttal there is incorporated herein by reference.

Hence, for applicant to suggest that Zhang's disclosure is non-enabling is quite remarkable.

Working examples: Zhang does not provide a working example of treating lymphomas in a patient. Neither does applicant.

Quantity of experimentation needed to treat lymphoma in a human based on the content of Zhang's disclosure:

Zhang discloses the dose, concentration, and the target disease. Clinical data with 20 year follow-up data is provided for one of three types of cancers Zhang explicitly teaches. CN 1121807 already disclosed to the public arsenic trioxide for lymphatic cancers. Simotsuura et al. already disclosed to the public antineoplasmic actions of arsenic trioxide. Li et al. already disclosed to the public arsenic trioxide-containing composition for treating malignant lymphomas. Not much experimentation would thus have been needed for one of ordinary skill in the art to have effectively treated lymphoma in a human. Simply following Zhang's disclosure would have produced the treatment, and the ordinary skilled artisan would have expected the same.

Therefore, it cannot be said that the ordinary skilled artisan would have had to resort to undue experimentation in order to obtain lymphoma treatment in a human by following Zhang's teachings. Consequently, applicant's arguments must be found unpersuasive and this ground of rejection must be maintained.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 9-11, 13-17 and 19-20 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Zhang (US 6,720,011) in view of CN 1121807 and Simotsuura et al. for the reasons of record – see the Office action of 12/15/2005, pages 4-6.

Applicant's arguments relative hereto have been given due consideration, but they were deemed unpersuasive. Applicant continues to argue that Zhang fails to provide any guidance as to efficacy of arsenic trioxide for the treatment of lymphoma. The Examiner's rebuttal of applicant's position is fully set forth above, and the discussion there is incorporated herein by reference. To reiterate in part, Zhang explicitly discloses (column 1, lines 33-35) (emphasis added):

> The present invention is directed to an intravenous drip composition for the treatment of cancers. The cancers treatable include leukemia, hepatoma and lymphoma.

Applicant further argues that the ordinary skilled artisan would not have had reasonable expectation of success. The Examiner cannot agree.

Zhang explicitly discloses treating lymphoma with arsenic trioxide (column 1, lines 34-45 and 41-43). IV composition containing 1-10 g arsenic trioxide, sodium

chloride and water is disclosed (column 1, lines 41-54). Effective daily dose of 10 ml of a composition containing 10 g/l of arsenic trioxide added to 500 ml of a 10% glucose solution is disclosed (column 2, lines 9-12), as well as a 0.1 wt% to 1 wt% arsenic trioxide containing compositions (column 2, lines 44-45). All such disclosures are in no way limited to leukemia treatment, as applicant may suggest. Those disclosures are broadly made with respect to all of Zhang's disclosed treatments. Hence, Zhang discloses the dose, concentration, and the target disease. Further, Zhang provides clinical data with 110 leukemia subjects, which data spans 20 years of follow-up results (columns 2-3, in particular column 3, lines 21-26). In contrast, it must be noted that applicant fails to provide any clinical data whatsoever in the instant application. Even though applicant claims treatment of "lymphoma in a human" (emphasis added), applicant fails to provide any clinical data. Hence, for applicant to suggest that Zhang's disclosure does not provide reasonable expectation of success but applicant's disclosure does is difficult to comprehend.

Additionally, CN 1121807 teaches arsenic trioxide for lymphatic cancers. Simotsuura et al. teach antineoplasmic actions of arsenic trioxide. Consequently, taken in combination, the cited references provide reasonable expectation of success.

Applicant's argument concerning busulfan, methotrexate, carmustine and lomustine are not even relevant to the present ground of rejection. Applicant greatly confuses the fact situation here. For applicant's argument to have any persuasive

weight, Zhang must have been silent as to lymphoma treatment and the Examiner must have been stretching a leukemia treatment disclosure to meet a lymphoma treatment claim. However, what makes this situation different from applicant's unpersuasive argument is that Zhang explicitly teaches treating lymphomas and CN 1121807 clearly teaches treatment of lymphatic cancers with arsenic trioxide. As a result, the fact that some other drugs were not known for one or more diseases is not relevant here. The distinguishing fact is that the cited prior art references clearly disclosed treatment of the disease for which applicant is now claiming.

Claims 9-11, 13-17 and 19-20 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Zhang in view of CN 1121807, Li et al. and Shimotsuura et al. for the reasons of record – see the Office action of 12/15/2005, pages 6-8.

It is noted that this ground of rejection is substantially the same in reasoning and prior art reliance as the previous ground of rejection under section 103. Applicant's arguments reflect this fact in relying on the same arguments and further criticizing the additional reference by Li et al. With respect to those same arguments, the Examiner's previous rebuttal in this Office action is incorporated herein by reference.

Li et al.[2] disclose treating 27 patients with malignant lymphoma, including Hodgkin's disease, with Ailin-1 (see the English translation on page 62). 70.37% remission rate reported (id.). Li et al. thus add to the previous discussion of the prior art in that they provide clinical report of 70.37% remission after treating 27 patients with

[2] Chinese J. Oncology, Vol. 10, pages 61-62 (1988).

malignant lymphoma, including Hodgkin's disease. The transliteration of Li's chemo-therapeutic formulation is "Ailin-1." From CN 1121807, it is known that "Ai Ling" formulations contain arsenic trioxide. It is the Examiner's position that the ordinary skilled person in the art of treating lymphatic cancers (including those artisans in the U.S. and China) would have recognized various transliterations such as "Ailin-1" and "Ai Ling" to be the same or similar Chinese formulations, which all contain arsenic trioxide. Hence, Li et al. add to the previously discussed body of knowledge concerning arsenic trioxide and lymphatic cancer efficacy by specifically teaching efficacy against malignant lymphomas, including Hodgkin's disease.

Applicant challenges the Examiner's reading of Li et al. by arguing that the composition of "Ailin-1" is not disclosed and thus the ordinary skilled artisan "could not have been known with certainty at the time of the invention due to the fact that its ingredients are not specified in the article." The Examiner cannot agree because applicant's position is in direct contradiction with the actual facts and also with applicant's own IDS. In good faith, applicant cannot make this argument in view of applicant's own IDS.

Applicant has cited in the parent and this application the following document:

> "Letter on Historical Facts Regarding the Development of Ai Ling No. 1 and the Clinical Use of Arsenic Trioxide in the Treatment of Acute Promyelocytic Leukemia and a Study of it Mechanism," Heilongjiang Branch of the Chinese Medical Association, Mar. 27, 1998.

The emphasis is on "Historical Facts." This document establishes that Ai-Ling No. 1 was known in China since 1971 as containing arsenic trioxide (page 1 of the document).

The cited article by Li et al. was published in 1988, and Li et al. were from the same hospital (Hospital of Harbin University) as where Ai-Ling No. 1 was developed. See page 1 of "Historical" document and affiliation of Li et al. in the article. Therefore, the Examiner's position is supported by applicant's submission of historical facts.

It is the Examiner's position that one of ordinary skill in this art would have recognized from the arsenic trioxide-containing Ai Ling of CN 1121807 that the transliteration "Ailin-1" in Li et al. also contained arsenic trioxide. Both references disclose lymphatic cancer treatments and the Ai Ling or "Ailin-1" compositions would have been recognized by the ordinary skilled artisan in this field as arsenic trioxide containing compositions.

For these reasons and for the reasons of record, this ground of rejection must be maintained.

In the preceding grounds of rejection, all ancillary references have been noted and discussed to rebut applicant's inaccurate statements regarding the state of the art. All previous grounds of prior art-based grounds of rejection are maintained.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to JOHN PAK whose telephone number is **(571)272-0620.** The Examiner can normally be reached on Monday to Friday from 8 AM to 4:30 PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's SPE, Johann Richter, can be reached on **(571)272-0646**.

The fax phone number for the organization where this application or proceeding is assigned is **(571)273-8300**.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571)272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JOHN PAK
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